

Remarks

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 2-11 and 33-37 are pending in the application, with claims 2 and 11 being the independent claims. Claims 1, 10 and 12-32 are sought to be cancelled without prejudice to or disclaimer of the subject matter therein, and claims 33-37 are sought to be added. These changes are believed to introduce no new matter, and their entry is respectfully requested. Support for new claims 33-37 can be found in the originally filed claims and on pages 20-22 of the specification. Support for the amendments in claims 2 and 11 can be found on page 14 of the specification.

Claims 33-37 are similar to claims 5-9, but depend on claim 2 instead of claim 1. Applicants respectfully request that these claims be examined because they are linked to a generic claim (claim 2) that Applicants believe is made allowable by the foregoing amendments and following remarks.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

I. Objection to the Specification

In the Office Action at page 2, the Examiner objected to the Title. By the foregoing amendment, Applicants amended the Title in accordance with the Examiner's suggestion.

In the Office Action at page 3, the Examiner objected to the Abstract for lack of narrative form. By the foregoing amendment, Applicants corrected the Abstract appropriately.

In the Office action at page 3, the Examiner stated that the Application is not in compliance with the sequence rules 37 C.F.R. §§ 1.821-1.825. Applicants respectfully disagree


with the objection. 37 C.F.R. § 1.821 requires that sequences of at least 4 amino acids in length, *specifically defined*, be given a sequence listing number and be identified by a SEQ ID NO. Specifically defined means those amino acids other than "Xaa" defined in accordance with the World Intellectual Property Organization, i.e. the sequence spelled out in the form XaaXaaXaaXaa *et cetera*. Applicants have spelled out the sequences and given them SEQ ID NOs. on pages 20-22. In addition, Applicants refer to these sequences by a name, such as [Ala¹]-hPTH(1-28), the way "albumin" would designate a gene of a particular sequence. Just as "albumin" would not require a SEQ ID NO. designation after it, so does [Ala¹]-hPTH(1-28) not require such a designation. Therefore, Applicants respectfully request that the objection to the specification be withdrawn.

II. Rejection under 35 U.S.C. § 101

In the Office Action at pages 3-4, the Examiner rejected claims 1-4 and 10-11 as directed to non-statutory matter because the claims read on a product of nature. By the foregoing amendments, claims 2, 3 and 11 were amended in accordance with the Examiner's suggestion, and claims 1 and 10 have been cancelled, thus rendering moot the portion of this rejection that may have applied to these claims.

III. Rejection under 35 U.S.C. § 112

In the Office Action at page 4, the Examiner rejected claims 1-4 and 10-11 under 35 U.S.C. § 112 for not reasonably providing enablement for all variants of SEQ ID NO: 1. By the foregoing amendments, claims 1 and 10 have been cancelled, thus rendering moot the portion of this rejection that may have applied to these claims. Applicants respectfully traverse the rejection as it may apply to the remaining claims.



The invention as claimed is directed to PTH minimized peptides and peptide derivatives with biological activity. The Examiner stated:

Due to the large quantity of experimentation required to determine how to use all variants of SEQ ID NO: 1, the lack of direction or guidance in the specification regarding same - e.g., the lack of guidance regarding specific activity of SEQ ID NO:1 with the first and nineteenth amino acid unspecified....the state of the art showing the unpredictability of function based on structural similarity of hormone polypeptides, and the breadth of the claims which embrace innumerable variants of SEQ ID NO:1, undue experimentation would be required of the skilled artisan to make and use the claimed invention in its full scope.

Office Action at 5.

If the Examiner's argument was intended to apply to the currently pending claims, Applicants respectfully disagree. Applicants limit the possible amino acid composition of the minimized polypeptides by using the term "consisting essentially of" rather than "comprising." In addition, Applicants provide specific amino acid substitutions at specific positions in these peptides. Applicants also provide data in the application showing that substituted polypeptides retain biological activity.

IV. First Rejection under 35 U.S.C. § 102

In the Office Action at page 6, the Examiner rejected claims 1-4 under 35 U.S.C. § 102(b) as being anticipated by Lewis *et al.* (U.K. Application GB 2,269,176-A) ["Lewis"]. By the forgoing amendment, claim 1 has been cancelled, thus rendering moot the portion of this rejection that may have applied to this claim. Applicants respectfully traverse this rejection as it may be applied to the remaining claims.

The invention as presently claimed is directed to minimized biologically active PTH peptides. In one aspect, the novelty of the present invention is the discovery that PTH peptides and peptide analogues shorter than 34 amino acids (aa) contain biological activity. Lewis describes and claims either a "PTH compound" in which the peptide has the native sequence and

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is chemically modified, or a "PTH compound" in which at least one amino acid in positions 1-38 in the native sequence is replaced. Lewis does not disclose an active PTH peptide that is shorter than 34 amino acids. The present invention relates to peptides having PTH activity that are 28 or fewer amino acids in length. Thus, Lewis does not disclose a key feature of the present invention.

Under 35 U.S.C. § 102, a claim can only be anticipated if every element in the claim is expressly or inherently disclosed in a single prior art reference. *See Kalman v. Kimberly Clark Corp.*, 713 F.2d 760, 771 (Fed. Cir. 1983), *cert. denied*, 465 U.S. 1026 (1984); *see also PPG Industries, Inc. v. Guardian Industries Corp.*, 75 F.3d 1558, 1566 (Fed. Cir. 1996) ("[t]o anticipate a claim, a reference must disclose every element of the challenged claim and enable one skilled in the art to make the anticipating subject matter."). In addition, under 35 U.S.C. § 102(b), a claim can only be anticipated by a publication if the publication describes the claimed invention with sufficient detail to place the public in possession of the invention. *See In re Donohue*, 766 F.2d 531, 533 (Fed. Cir. 1985). Applicants respectfully assert that Lewis does not support a rejection of the invention as presently claimed under 35 U.S.C. § 102(b).

V. Second Rejection under 35 U.S.C. § 102

In the Office Action at page 6, the Examiner rejected claims 1-4 under 35 U.S.C. § 102(b) as being anticipated by Willick *et al.* (U.S. Patent No. 5,556,940) ["Willick"]. By the foregoing amendments, claim 1 has been cancelled, thus rendering moot the portion of this rejection that may have applied to this claim. Applicants respectfully traverse this rejection as it may be applied to the remaining claims.

The present invention relates to PTH peptides substituted at position 1 and 19, and the claims specifically exclude peptides with wild type sequence of human PTH (hPTH). Willick

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discloses hPTH(1-28)-NH₂ (wild type sequence) and [Leu²⁷]-hPTH(1-28)-NH₂ (substituted at position 27). Thus, Willick fails to disclose expressly or inherently the biologically active PTH peptides of the present invention. Hence, under *Kalman*, *PPG Industries*, and *Donohue*, Willick cannot and does not anticipate the presently claimed invention. Applicants therefore respectfully assert that Willick does not support a rejection of the invention as presently claimed under 35 U.S.C. § 102(b).

VI. Third Rejection under 35 U.S.C. § 102

In the Office Action at page 6, the Examiner rejected claims 1-4 under 35 U.S.C. § 102(b) as being anticipated by Chu *et al.* (Biochem. 14:3631) ["Chu"]. By the foregoing amendments, claim 1 has been cancelled, thus rendering moot the portion of this rejection that may have applied to this claim. Applicants respectfully traverse this rejection as it may be applied to the remaining claims.

As discussed above, the present invention relates to PTH peptides substituted at positions 1 and 19, and the claims specifically exclude peptides with wild type sequence of hPTH. Chu discloses the wild type sequences of the first 24 amino acids of PTH from three species, including hPTH, but Chu does not disclose any substitutions of the native sequences. Therefore, Chu, like Willick, does not disclose the biologically active PTH peptides of the present invention. Therefore, under *Kalman*, *PPG Industries*, and *Donohue*, Kramer cannot and does not anticipate the presently claimed invention. Applicants therefore respectfully assert that Chu does not support a rejection of the invention as presently claimed under 35 U.S.C. § 102(b).

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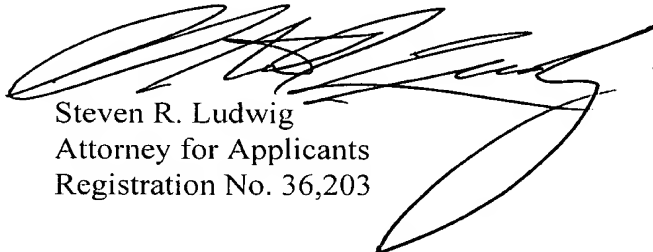
Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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Version with markings to show changes made

In the Claims:

Claims 1, 10 and 12-32 are sought to be cancelled without prejudice or disclaimer.

Claims 33-37 are sought to be added.

2. (Once amended) An isolated biologically active peptide consisting essentially of the formula:

(b) X_{01} ValSerGluIleGlnLeuMetHisAsnLeuGlyLysHisLeuAsnSerMet X_{02}

ArgValGluTrpLeuArgLysLysLeu (SEQ ID NO:1);

(c) fragments thereof containing amino acids 1-24, 1-25, 1-26 or 1-27;

(d) pharmaceutically acceptable salts thereof; or

(e) N- or C- derivatives thereof;

wherein:

X_{01} is Ser, Ala or Gly; and

X_{02} is Glu or Arg,

provided that said peptide is not hPTH(1-27)NH₂ or hPTH(1-28)NH₂.

3. (Once amended) The peptide of claim 2 [1], wherein the peptide is labeled with a label selected from the group consisting of: radiolabel, fluorescent label, bioluminescent label or chemiluminescent label.

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11. (Once amended) A pharmaceutical composition comprising

- (a) an isolated biologically active peptide consisting essentially of the

formula:

X_{01} ValSerGluIleGlnLeuMetHisAsnLeuGlyLysHisLeuAsnSerMet X_{02}

ArgValGluTrpLeuArgLysLysLeu (SEQ ID NO:1);

- (b) fragments thereof containing amino acids 1-24, 1-25, 1-26 or 1-27;
(c) pharmaceutically acceptable salts thereof; or
(d) N- or C- derivatives thereof;

wherein:

X_{01} is Ser, Ala or Gly; and

X_{02} is Glu or Arg.

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